

1/13

Figure 1

Pfu	10	MILDVDYITEEGKPV	20	IRL	30	EHDRITFRPYIYALL	40	RRDDSK	50	IEVKKITG	60	ERHGG
DeepVent		MILDADYITEEDGKPI		IRI		EHDRITFRPYIYALL		KDDSSQ		IDEVKKITAE		ERHGG
Hybrid_design		MILDXDYITEEXGKPI		IRX		EHDRITFRPYIYALL		XDDSSX		IXEVKKITXX		ERHGG
Pfu	70	KIVRIIVDVKEKVE	80	PI	90	TVWKL	100	REHPPAVV	110	DI	120	FEYDIPFAKRY
DeepVent		KIVRIIDAEKVR		GRPI		EVWRL		REHPPAVV		DI		FEYDIPFAKRY
Hybrid_design		KIVRIIXDXEKV		LGXP		IXVWXL		REHPPAVV		DI		FEYDIPFAKRY
Pfu	130	LIDKGLIPMEGEGEEL	140	LLAFDIET	150	LYHEGEEFF	160	IMISYADE	170	NEAKVITWKN	180	IDLPPY
DeepVent		LIDKGLIPMEGDEEL		LLAFDIET		LYHEGEEFF		IMISYADE		NEAKVITWKN		IDLPPY
Hybrid_design		LIDKGLIPMEGXEEL		LLAFDIET		LYHEGEEFF		IMISYADE		NEAKVITWKN		IDLPPY
Pfu	190	VEVVSSEMEREMIKR	200	FLRI	210	IVTYNGDSFD	220	FPYLLAKRAEKL	230	GIKLTI	240	GRDGSSEPK
DeepVent		VEVVSSEMEREMIKR		FLKVI		IVTYNGDSFD		FPYLLAKRAEKL		GIKLTI		GRDGSSEPK
Hybrid_design		VEVVSSEMEREMIKR		FLXXI		IVTYNGDSFD		FPYLLAKRAEKL		GIKLTI		GRDGSSEPK
Pfu	250	MQRIGDMTAVEV	260	VKGRIFHFDLY	270	IVHVI	280	RTINLPT	290	YTL	300	EA
DeepVent		MQRIGDMTAVEI		VKGRIFHFDLY		IVHVI		RTINLPT		YTL		EA
Hybrid_design		MQRIGDMTAVEX		VKGRIFHFDLY		IVHVI		RTINLPT		YTL		EA
Pfu	310	SGENLERVAKYSMED	320	AKATYELG	330	KREFL	340	PMEL	350	IQLSRLV	360	QPLWDVSRSS
DeepVent		TGKGLERVAKYSMED		AKATYELG		KREFL		PMEL		QPLWDVSRSS		STGNLVEWFL
Hybrid_design		XGXGLERVAKYSMED		AKATYELG		KREFL		PMEL		QPLWDVSRSS		STGNLVEWFL
Pfu	370	AYERNELVAPNKP	380	PS	390	EEYQRRRLRES	400	YTG	410	FFVKEPEKGLWE	420	NI
DeepVent		AYERNELVAPNKP		PS		EEYQRRRLRES		YTG		FFVKEPEKGLWE		NI
Hybrid_design		AYERNELVAPNKP		PS		EEYQRRRLRES		YTG		FFVKEPEKGLWE		NI
Pfu	430	PDTLNL	440	LEGCKNYD	450	IA	460	PQ	470	VGHKFFCKD	480	I
DeepVent		PDTLNL		LEGCKNYD		IA		PQ		VGHKFFCKD		I
Hybrid_design		PDTLNL		LEGCKNYD		IA		PQ		VGHKFFCKD		I

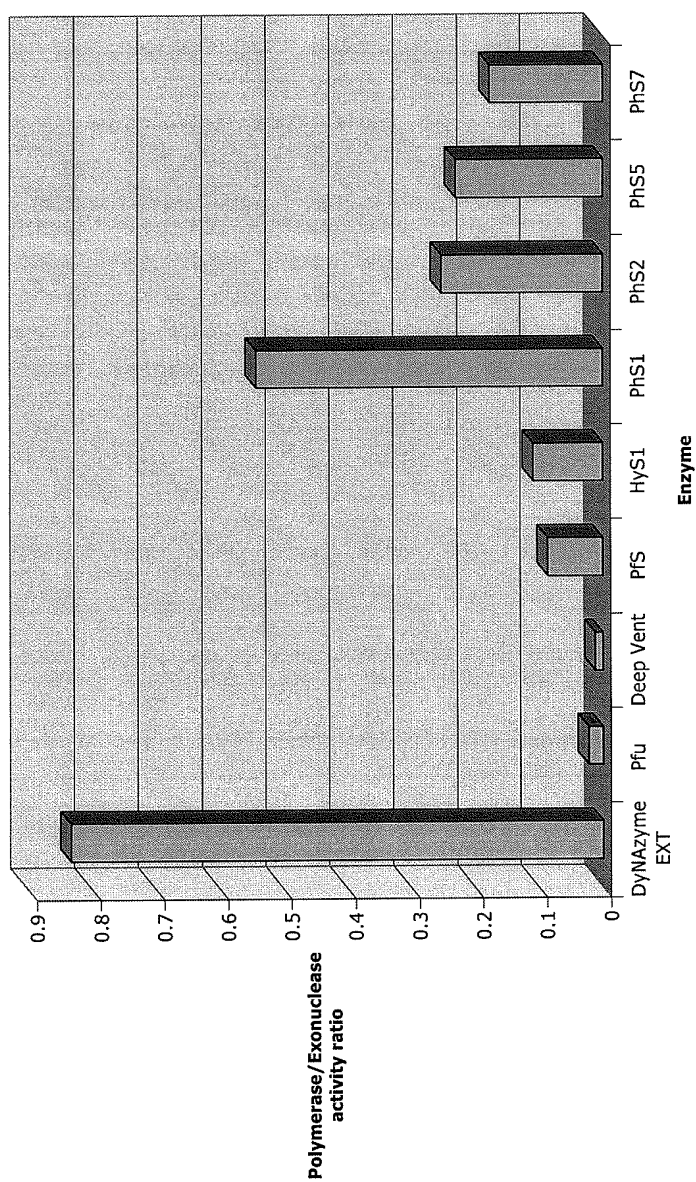
Figure 1 (cont'd)

Pfu
DeepVent
Hybrid_design

Figure 2. Assembly of the oligonucleotides into library fragments.

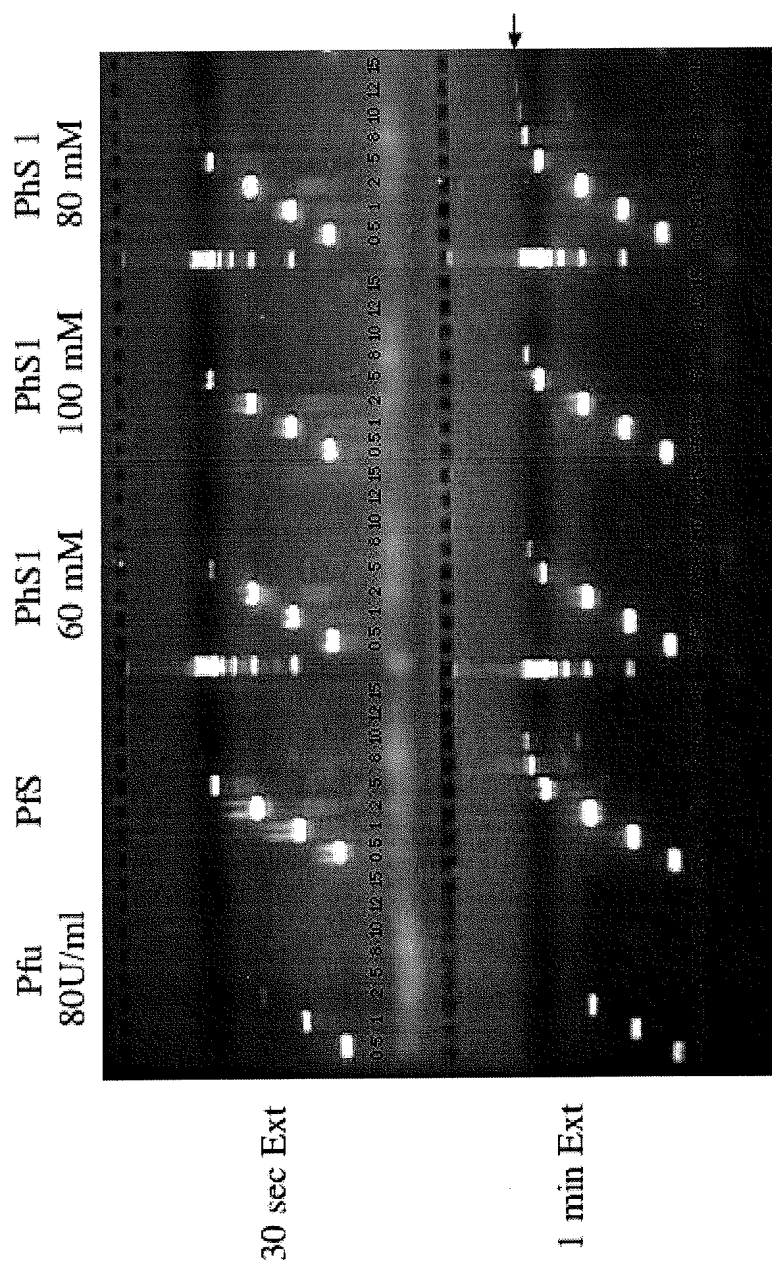
4/13

Figure 3. A comparison of the polymerase to 3' to 5' exonuclease activity



5/13

FIGURE 4



6/13

Figure 5

Pfu	10	20	30	40	50	60
DeepVent	MIL	DDV	DDY	DDY	DDY	DDY
Hybrid_design	MIL	DDV	DDY	DDY	DDY	DDY
HyS1	MIL	DDV	DDY	DDY	DDY	DDY
Hyb2	MIL	DDV	DDY	DDY	DDY	DDY
Hyb3	MIL	DDV	DDY	DDY	DDY	DDY
HyS4	MIL	DDV	DDY	DDY	DDY	DDY
PhS1	MIL	DDV	DDY	DDY	DDY	DDY
PhS2	MIL	DDV	DDY	DDY	DDY	DDY
PhS3	MIL	DDV	DDY	DDY	DDY	DDY
PhS4	MIL	DDV	DDY	DDY	DDY	DDY
PhS5	MIL	DDV	DDY	DDY	DDY	DDY
PhS6	MIL	DDV	DDY	DDY	DDY	DDY
PhS7	MIL	DDV	DDY	DDY	DDY	DDY

Pfu	70	80	90	100	110	120
DeepVent	KIV	RIV	IVD	IVD	IVD	IVD
Hybrid_design	KIV	RIV	IVD	IVD	IVD	IVD
HyS1	KIV	RIV	IVD	IVD	IVD	IVD
Hyb2	KIV	RIV	IVD	IVD	IVD	IVD
Hyb3	KIV	RIV	IVD	IVD	IVD	IVD
HyS4	KIV	RIV	IVD	IVD	IVD	IVD
PhS1	KIV	RIV	IVD	IVD	IVD	IVD
PhS2	KIV	RIV	IVD	IVD	IVD	IVD
PhS3	KIV	RIV	IVD	IVD	IVD	IVD
PhS4	KIV	RIV	IVD	IVD	IVD	IVD
PhS5	KIV	RIV	IVD	IVD	IVD	IVD
PhS6	KIV	RIV	IVD	IVD	IVD	IVD
PhS7	KIV	RIV	IVD	IVD	IVD	IVD

pfu DeepVent Hybrid_design HyS1 Hyb2 Hyb3 HyS4 PhS1 PhS2 PhS3 PhS4 PhS5 PhS6 PhS7

Pfu
DeepVent
Hybrid_design
HyS1
Hyb2
Hyb3
HyS4
PhS1
PhS2
PhS3
PhS4
PhS5
PhS6
PhS7

8/13

Figure 5 (cont'd)

Pfu	250	260	270	280	290	300
DeepVent	IGDMT	AVV	KGR	IHF	DL	YHVI
Hybrid_design	IGDMT	AVV	KGR	IHF	DL	YHVI
HyS1	IGDMT	AVV	KGR	IHF	DL	YHVI
Hyb2	IGDMT	AVV	KGR	IHF	DL	YHVI
Hyb3	IGDMT	AVV	KGR	IHF	DL	YHVI
HyS4	IGDMT	AVV	KGR	IHF	DL	YHVI
PhS1	IGDMT	AVV	KGR	IHF	DL	YHVI
PhS2	IGDMT	AVV	KGR	IHF	DL	YHVI
PhS3	IGDMT	AVV	KGR	IHF	DL	YHVI
PhS4	IGDMT	AVV	KGR	IHF	DL	YHVI
PhS5	IGDMT	AVV	KGR	IHF	DL	YHVI
PhS6	IGDMT	AVV	KGR	IHF	DL	YHVI
PhS7	IGDMT	AVV	KGR	IHF	DL	YHVI

Pfu	310	320	330	340	350	360
DeepVent	SGEN	LER	VAK	YSM	EDAK	ATY
Hybrid_design	SGEN	LER	VAK	YSM	EDAK	ATY
HyS1	SGEN	LER	VAK	YSM	EDAK	ATY
Hyb2	SGEN	LER	VAK	YSM	EDAK	ATY
Hyb3	SGEN	LER	VAK	YSM	EDAK	ATY
HyS4	SGEN	LER	VAK	YSM	EDAK	ATY
PhS1	SGEN	LER	VAK	YSM	EDAK	ATY
PhS2	SGEN	LER	VAK	YSM	EDAK	ATY
PhS3	SGEN	LER	VAK	YSM	EDAK	ATY
PhS4	SGEN	LER	VAK	YSM	EDAK	ATY
PhS5	SGEN	LER	VAK	YSM	EDAK	ATY
PhS6	SGEN	LER	VAK	YSM	EDAK	ATY
PhS7	SGEN	LER	VAK	YSM	EDAK	ATY

9/13

Figure 5 (cont'd)

Pfu	370	AYERNEL	AVAPNKKPP	EE	EYER	QRRRL	RRRLRES	YTG	GGY	FF	VKEPE	KGLWEN	IV	YLD	DFRSL	YPPS	II	ITH	NVS	420
DeepVent		AYERNEL	LAPNKKPP	DE	EYER	RRRL	RRRLRES	YAG	GGY	XX	VKEPE	KGLWEN	GL	VS	LDFRSL	YPPS	II	ITH	NVS	
Hybrid_design		AYERNEL	EXAPNKKPP	EX	EYER	RRRL	RRRLRES	YX	GGY	XX	VKEPE	KGLWEN	XX	VS	LDFRSL	YPPS	II	ITH	NVS	
HyS1		AYERNEL	AVAPNKKPP	YER	EYER	RRRL	RRRLRES	YTG	GGY	FF	VKEPE	KGLWEN	VS	LDFRSL	YPPS	II	ITH	NVS		
Hyb2		AYERNEL	AVAPNKKPP	AE	EYER	RRRL	RRRLRES	YTG	GGY	FF	VKEPE	KGLWEN	VS	LDFRSL	YPPS	II	ITH	NVS		
Hyb3		AYERNEL	AVAPNKKPP	AE	EYER	RRRL	RRRLRES	YTG	GGY	FF	VKEPE	KGLWEN	VS	LDFRSL	YPPS	II	ITH	NVS		
HyS4		AYERNEL	AVAPNKKPP	AE	EYER	RRRL	RRRLRES	YTG	GGY	FF	VKEPE	KGLWEN	VS	LDFRSL	YPPS	II	ITH	NVS		
PhS1		AYERNEL	AVAPNKKPP	DE	EYER	RRRL	RRRLRES	YAG	GGY	FF	VKEPE	KGLWEN	IV	YLD	DFRSL	YPPS	II	ITH	NVS	
PhS2		AYERNEL	AVAPNKKPP	SE	EYER	RRRL	RRRLRES	YTG	GGY	FF	VKEPE	KGLWEN	IV	YLD	DFRSL	YPPS	II	ITH	NVS	
PhS3		AYERNEL	AVAPNKKPP	SE	EYER	RRRL	RRRLRES	YAG	GGY	FF	VKEPE	KGLWEN	IV	YLD	DFRSL	YPPS	II	ITH	NVS	
PhS4		AYERNEL	AVAPNKKPP	DE	EYER	RRRL	RRRLRES	YTG	GGY	FF	VKEPE	KGLWEN	VS	LDFRSL	YPPS	II	ITH	NVS		
PhS5		AYERNEL	AVAPNKKPP	DE	EYER	RRRL	RRRLRES	YTG	GGY	FF	VKEPE	KGLWEN	VS	LDFRSL	YPPS	II	ITH	NVS		
PhS6		AYERNEL	AVAPNKKPP	DE	EYER	RRRL	RRRLRES	YTG	GGY	FF	VKEPE	KGLWEN	VS	LDFRSL	YPPS	II	ITH	NVS		
PhS7		AYERNEL	AVAPNKKPP	DE	EYER	RRRL	RRRLRES	YTG	GGY	FF	VKEPE	KGLWEN	VS	LDFRSL	YPPS	II	ITH	NVS		

Pfu	430	P	D	T	L	N	L	E	G	C	K	N	Y	D	I	A	P	Q	V	G	H	K	F	C	K	D	I	P	G	F	I	P	S	L	L	G	H	L	L	E	E	R	Q	K	I	K	T	K	M	K	A	S	K	E	T	Q	D	P	I	E	K	I	L	L	480																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																															
DeepVent		P	D	T	L	N	R	E	G	C	K	R	E	Y	D	V	A	P	Q	V	G	H	K	F	C	K	D	F	P	G	F	I	P	S	L	L	K	R	L	L	D	E	R	Q	E	I	K	R	K	M	K	A	S	K	D	P	I	E	K	K	M	L																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																		
Hybrid_design		P	D	T	L	N	X	E	G	C	K	X	Y	D	X	A	P	Q	V	G	H	K	F	C	K	D	X	F	P	G	F	I	P	S	L	L	X	X	L	L	X	E	R	Q	X	I	K	X	K	M	K	X	X	X	D	P	I	E	K	X	X	L																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																		
HyS1		P	D	T	L	N	R	E	G	C	K	D	Y	D	I	A	P	Q	V	G	H	K	F	C	K	D	F	L	G	F	I	P	S	L	L	G	H	L	L	E	E	R	Q	E	I	K	T	K	M	K	E	T	X	D	P	I	E	K	I	L	L																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																			
Hyb2		P	D	T	L	N	R	E	G	C	K	D	Y	D	I	A	P	Q	V	G	H	K	F	C	K	D	F	L	G	F	I	P	S	L	L	G	H	L	L	E	E	R	Q	E	I	K	T	K	M	K	E	T	X	D	P	I	E	K	I	L	L																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																			
Hyb3		P	D	T	L	N	R	E	G	C	K	D	Y	D	I	A	P	Q	V	G	H	K	F	C	K	D	F	L	G	F	I	P	S	L	L	G	H	L	L	E	E	R	Q	E	I	K	T	K	M	K	E	T	X	D	P	I	E	K	I	L	L																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																			
HyS4		P	D	T	L	N	R	E	G	C	K	D	Y	D	I	A	P	Q	V	G	H	K	F	C	K	D	F	L	G	F	I	P	S	L	L	G	H	L	L	E	E	R	Q	E	I	K	T	K	M	K	E	T	X	D	P	I	E	K	I	L	L																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																			
PhS1		P	D	T	L	N	R	E	G	C	K	R	N	Y	D	V	A	P	Q	V	G	H	K	F	C	K	D	F	P	G	F	I	P	S	L	L	K	R	L	L	D	E	R	Q	K	I	K	T	K	M	K	A	S	K	D	P	I	E	K	I	M	L																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																		
PhS2		P	D	T	L	N	L	E	G	C	K	E	Y	D	V	A	P	Q	V	G	H	K	F	C	K	D	I	P	G	F	I	P	S	L	L	G	H	L	L	E	E	R	Q	K	I	K	R	K	M	K	A	S	K	D	P	I	E	K	I	L	L																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																			
PhS3		P	D	T	L	N	R	E	G	C	K	N	Y	D	I	A	P	Q	V	G	H	K	F	C	K	D	I	P	G	F	I	P	S	L	L	K	H	L	L	D	E	R	Q	K	I	K	R	K	M	K	E	S	K	D	P	I	E	K	K	M	L																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																			
PhS4		P	D	T	L	N	R	E	G	C	K	E	Y	D	I	A	P	Q	V	G	H	K	F	C	K	D	F	P	G	F	I	P	S	L	L	K	H	L	L	D	E	R	Q	K	I	K	R	K	M	K	A	S	K	D	P	I	E	K	K	M	L																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																			
PhS5		P	D	T	L	N	R	E	G	C	K	E	Y	D	V	A	P	Q	V	G	H	K	F	C	K	D	F	P	G	F	I	P	S	L	L	K	R	L	L	D	E	R	Q	K	I	K	R	K	M	K	A	T	N																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																											</

10/13

Figure 5 (cont'd)

Pfu	490	DYRQKAIKLLANS	FYGYGYAKARWYCKE	CAESVTAWGR	KYIELVW	KEL	EEK	FGFK	VLYI	540
DeepVent		RRAIKLLANS	YGYGYAKARWYCKE	CAESVTAWGR	EYIEFV	RKEL	EEK	FGFK	VLYI	
Hybrid_design		QXAIKLLANS	XYGYGYAKARWYCKE	CAESVTAWGR	XYIEFV	XKEL	EEK	FGFK	VLYI	
HyS1		QKAIKLLANS	YGYGYAKARWYCKE	CAESVTAWGR	EYIEFV	WKEL	EEK	FGFK	VLYI	
Hyb2		QKAIKLLANS	YGYGYAKARWYCKE	CAESVTAWGR	EYIEFV	WKEL	EEK	FGFK	VLYI	
Hyb3		QKAIKLLANS	YGYGYAKARWYCKE	CAESVTAWGR	EYIEFV	WKEL	EEK	FGFK	VLYI	
HyS4		QKAIKLLANS	YGYGYAKARWYCKE	CAESVTAWGR	EYIEFV	WKEL	EEK	FGFK	VLYI	
PhS1		QKAIKLLANS	YGYGYAKARWYCKE	CAESVTAWGR	EYIEFV	WKEL	EEK	FGFK	VLYI	
PhS2		QKAIKLLANS	FYGYGYAKARWYCKE	CAESVTAWGR	EYIELV	RKEL	EEK	FGFK	VLYI	
PhS3		QRAIKLLANS	YGYGYAKARWYCKE	CAESVTAWGR	EYIEFV	RKEL	EEK	FGFK	VLYI	
PhS4		QRAIKLLANS	FYGYGYAKARWYCKE	CAESVTAWGR	EYIELV	WKEL	EEK	FGFK	VLYI	
PhS5		QRAIKLLANS	FYGYGYAKARWYCKE	CAESVTAWGR	EYIELV	WKEL	EEK	FGFK	VLYI	
PhS6		QRAIKLLANS	FYGYGYAKARWYCKE	CAESVTAWGR	EYIELV	WKEL	EEK	FGFK	VLYI	
PhS7		QRAIKLLANS	FYGYGYAKARWYCKE	CAESVTAWGR	EYIELV	WKEL	EEK	FGFK	VLYI	

Pfu	550	DTDGLYATIPGG	ES	EEIKKKKALEFV	KYIN	SKLPG	LLELEY	EGFY	KRG	FFVT	KKRYA	VIDE
DeepVent		DTDGLYATIPGG	AK	PEEIKKKALEFV	DYIN	AKLPG	LLELEY	EGFY	VRG	FFVT	KKRYA	VIDE
Hybrid_design		DTDGLYATIPGG	XX	EEIKKKKALEFV	KYIN	YKLPG	LLELEY	EGFY	XRG	FFVT	KKRYA	VIDE
HyS1		DTDGLYATIPGG	EE	PEEIKKKALEFV	KYIN	SKLPG	LLELEY	EGFY	KRG	FFVT	KKRYA	VIDE
Hyb2		DTDGLYATIPGG	EE	PEEIKKKALEFV	KYIN	SKLPG	LLELEY	EGFY	KRG	FFVT	KKRYA	VIDE
Hyb3		DTDGLYATIPGG	EE	PEEIKKKALEFV	KYIN	SKLPG	LLELEY	EGFY	KRG	FFVT	KKRYA	VIDE
HyS4		DTDGLYATIPGG	EE	PEEIKKKALEFV	KYIN	SKLPG	LLELEY	EGFY	KRG	FFVT	KKRYA	VIDE
PhS1		DTDGLYATIPGG	KS	PEEIKKKALEFV	DYIN	AKLPG	LLELEY	EGFY	KRG	FFVT	KKRYA	VIDE
PhS2		DTDGLYATIPGG	KS	PEEIKKKALEFV	DYIN	SKLPG	LLELEY	EGFY	KRG	FFVT	KKRYA	VIDE
PhS3		DTG-LYATIPGA	KS	EEIKKKKALEFV	KYIN	SKLPG	LLELEY	EGFY	VRG	FFVT	KKRYA	VIDE
PhS4		DTDGLYATIPGG	K	PEEIKKKALEFV	KYIN	SKLPG	LLELEY	EGFY	VRG	FFVT	KKRYA	VIDE
PhS5		DTDGLYATIPGG	K	PEEIKKKALEFV	KYIN	SKLPG	LLELEY	EGFY	VRG	FFVT	KKRYA	VIDE
PhS6		DTDGLYATIPGG	K	PEEIKKKALEFV	KYIN	SKLPG	LLELEY	EGFY	VRG	FFVT	KKRYA	VIDE
PhS7		DTDGLYATIPGG	K	PEEIKKKALEFV	KYIN	SKLPG	LLELEY	EGFY	VRG	FFVT	KKRYA	VIDE

11/13

Figure 5 (cont'd)

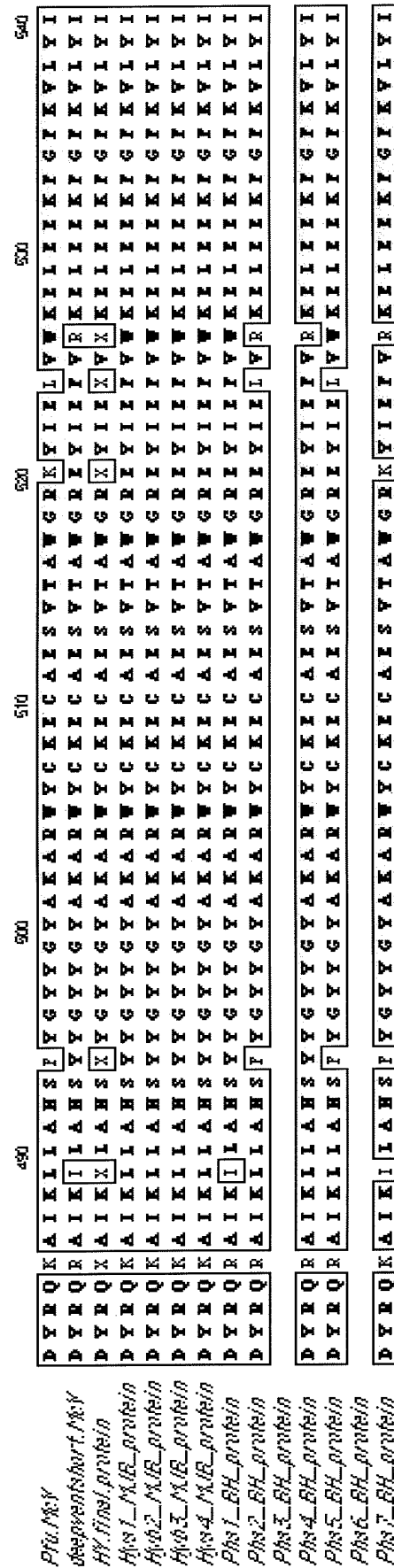
Pfu	610	EGKVI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	TI	LK	HGN	VEE	AV	RI	VK	EV	IQ	KL	AN	YE	IE	PP	EK	580
DeepVent		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	
Hybrid_design		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	
HyS1		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	
Hyb2		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	
Hyb3		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	
HyS4		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	
PhS1		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	
PhS2		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	
PhS3		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	
PhS4		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	
PhS5		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	
PhS6		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	
PhS7		EGKI	ITR	GLE	EIV	RR	DW	SEI	AK	ET	QAR	VLE	AI	LK	HGN	VEE	AV	RI	VK	EV	TE	KL	SK	YE	IE	PP	EK	

pfu	670	L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	720
DeepVent		L	V	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	
Hybrid_design		L	X	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	
HyS1		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	
Hyb2		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	
Hyb3		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	
HyS4		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	
PhS1		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	
PhS2		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	
PhS3		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	
PhS4		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	
PhS5		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	
PhS6		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	
PhS7		L	A	I	Y	E	Q	I	T	R	P	L	H	E	Y	K	A	I	G	P	H	V	A	V	A	K	K	L	A	A	R	G	V	K	I	K	P	G	M	V	I	G	Y	I	V	L	R	G	D	G	P	I	S	N	R	A	I	L	A	E	E	

Pfu	DeepVent	Hybrid_design	790	800	810	820	830	840
HyS1	N H D	G A T V K F K Y K G E E K E V D I S K I K K V W R V G K M I S F T Y D E G G G K T G R G A V S E K D A P K E L L Q M L E						
Hyb2								
Hyb3								
HyS4								
PhS1								
PhS2								
PhS3								
PhS4								
PhS5								
PhS6								
PhS7								

Pfu
DeepVent
Hybrid_design
HyS1
Hyb2
Hyb3
HyS4
PhS1
PhS2
PhS3
PhS4
PhS5
PhS6
PhS7

Figure 6



**Invariable sequence element (24 aa) in hybrid proteins
(contains nucleotide binding motif)**